IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ACCORD HEALTHCARE INC., ET AL., Defendants.	C.A. No. 18-1043-KAJ

NOVARTIS'S POST-TRIAL BRIEF ON
THE VALIDITY OF U.S. PATENT NO. 9,187,405

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GLOSSARY

Term	Definition
405 Patent, or Patent	U.S. Pat. No. 9,187,405, the Patent-in-Suit (D.I. 715, PTO Ex. 1 ¶ 9)
ANDA	"Abbreviated New Drug Application" submitted under 21 U.S.C. § 355(j)
NCOL	Novartis's Proposed Conclusions of Law (Submitted April 10 and May 8, 2020)
EAE	Expermiental Autoimmune (or Allergic) Encephalomyelitis, an animal model of multiple sclerosis (*see, e.g.,* Tr. at 338:12–18, 922:3–6)
FDA	U.S. Food and Drug Administration
FRCP	The Federal Rules of Civil Procedure
FRE	The Federal Rules of Evidence
HCOL	HEC's Proposed Conclusions of Law (Submitted April 10, 2020)
HEC	Defendants HEC Pharm Co., Ltd. and HEC Pharm USA Inc. (D.I. 715, PTO Ex. 1 ¶¶ 2–3)
HEC Br.	HEC's April 10, 2020 Validity Brief (D.I. 743)
HFOF	HEC's Proposed Findings of Fact (Submitted April 10, 2020)
IPR	Inter-partes Review under 35 U.S.C. § 311, et seq.
IPR FWD	Final Written Decision issued in IPR2017-00854 (D.I. 1, Ex. B)
MS	Multiple sclerosis
NFOF	Novartis's Proposed Findings of Fact (Submitted April 10 and May 8, 2020)

GLOSSARY
(continued)

Novartis	Plaintiff Novartis Pharmaceuticals Corporation (D.I. 715, PTO Ex. 1 ¶ 1)
Orange Book	U.S. Food and Drug Administration, Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). www.fda.gov/drugs/informationondrugs/ucm129662.htm. (*See* 21 U.S.C. § 355(b)(1), (j)(7)(A); 21 C.F.R. § 314.53.)
Patent Office	U.S. Patent and Trademark Office
PI	Preliminary Injunction
PTAB	Patent Trial and Appeals Board of the Patent Office
PTO	The Pre-Trial Order Submitted February 7, 2020 (D.I. 715)
RRMS	Relapsing-remitting multiple sclerosis
Paragraph IV Letter	Notice provided under 21 U.S.C. § 355(j)(2)(A)(vii)(IV)
Tr.	Transcript to the March 2–5 trial in this matter (D.I. 738–741)

PRELIMINARY STATEMENT

The 405 Patent enjoys a strong presumption of validity after being upheld over IPR challenges at the Patent Office and in a preliminary injunction in this case. Nonetheless, HEC challenges validity here with arguments largely recycled from those proceedings. HEC contends the Patent claims lack written description for reasons contrary to the Patent's plain language and based on arguments rejected in the IPR. HEC also alleges anticipation by Kappos 2006, a reference the Court rejected as not anticipatory in the PI. HEC comes nowhere close to providing clear and convincing evidence of invalidity, including because the complete perspective of the person of skill is missing from HEC's case. The Court should enter judgment for Novartis.

Inventors Peter Hiestand and Christian Schnell used the well-established EAE rat model of MS in a new way, discovering that far less fingolimod could be used to treat RRMS than had been thought necessary. Novartis filed a patent application on this discovery in Great Britain on June 27, 2006 that described the inventors' EAE results and explicitly recited a 0.5 mg daily dose in a human RRMS treatment example. The identical application was re-filed in the U.S. patent system, and the Patent Office ultimately granted the 405 Patent with claims to the treatment of RRMS by administering 0.5 mg of fingolimod daily absent an immediately preceding loading dose. Gilenya®, a blockbuster RRMS medicine, is an embodiment of that invention.

Written Description: The 405 Patent provides ample support for the claimed treatment method. The entire Patent is focused on the treatment of demyelinating diseases such as RRMS. The Patent's title is "S1P Receptor Modulators for Treating Relapsing-Remitting Multiple Sclerosis," and fingolimod is specifically highlighted as a preferred compound. The Patent also contains two examples: a working example with results from an EAE animal model showing that less fingolimod than previously thought possible could treat relapses in rats, and a human prophetic

example explicitly describing the use of 0.5 mg fingolimod to treat RRMS. Section 112 demands no more for written description.

HEC, however, says more was needed for two claim elements: the treatment purpose of the 0.5 mg daily dose and the absence of an immediately preceding loading dose regimen.

The Treatment Purpose of the 0.5 mg Daily Dose. HEC argues that the EAE example does not support the claims' recitation of treatment of human RRMS with 0.5 mg daily—even though the human prophetic example spells out that exact treatment. HEC is hamstrung in addressing the human example because it failed to offer any physician testimony on it at trial—HEC's physician witness refused to testify about that part of the Patent. HEC thus lacks the perspective of the full person of skill in this case; as the parties agree, that "person" is a team that includes an MS clinician. Without that perspective, HEC is forced to rely on attorney argument, which is manifestly insufficient, including for reasons the Court already set out in granting the PI: "A patent does not need to tell the full story or really even any story about how the inventors came to their invention, and it need not state things that a POSA would already know, including the prior art. Much of the defendants' attack on the supposed lack of adequate written description is really legal irrelevancies, therefore." (D.I. 583 at 6.) The specification's clear recitation of initially administering a 0.5 mg daily dose to treat RRMS in humans is all that is needed.

The Loading Dose Exclusion. HEC again ignores the specification's plain terms in arguing that the absence of a loading dose is unsupported. As Novartis's experts testified, the specification's description of a "daily" dose given "initially" precludes the use of a loading dose, which the parties agree is a greater-than-normal dose given at the beginning of therapy.

The Patent Office rejected HEC's exact argument in the IPR, and this Court reiterated that finding in granting the PI. (D.I. 583 at 6.) But HEC says those decisions were wrong under

Santarus, Inc. v. Par Pharm., Inc., 694 F.3d 1344 (Fed. Cir. 2012), which HEC contends requires that a patent *must* describe a "reason to exclude" a negative limitation. This is incorrect. The law only demands sufficient description to show a person of skill that the inventors had possession of the invention. *Santarus* did not create a heightened standard for written description support of negative limitations. It states that a patent can describe a negative claim limitation by providing a reason to exclude, but there are other ways to do so too. Here, ample proof at trial showed that a person of skill would read the human example and understand the inventors possessed the dosing regimen of 0.5 mg fingolimod daily without a loading dose. Even if HEC's "reason to exclude" standard applied, the Patent specification provides reasons to exclude a loading dose.

HEC's brief pins its hopes on the Federal Circuit oral argument in the IPR appeal, apparently hoping the IPR decision would be overturned. But the transcript is neither a binding opinion nor relevant evidence here, and in any event the Federal Circuit dismissed the IPR appeal on April 23, 2020. *Argentum Pharm. LLC v. Novartis Pharm. Corp.*, No. 2018-2273, 2020 WL 1944759 (Fed. Cir. Apr. 23, 2020). The IPR decision upholding the 405 Patent is now final, and disposes of HEC's argument.

The Patent's Novelty. HEC says Kappos 2006, a short abstract announcing the design of an upcoming Phase III trial, anticipated the claimed invention. (DTX-47.) This challenge fails from the start because HEC never proved, as it must, that Kappos 2006 was publicly accessible prior to the Patent being filed. Proving that Kappos 2006 is prior art is HEC's burden. HEC offered a declaration from a British Library employee but, after argument at trial, the Court excluded it as inadmissible hearsay. HEC now asks for a do-over on that ruling, but it is too late as Novartis would now be prejudiced by a change in course. HEC then resorts to a patchwork of trial testimony attempting, yet failing, to prove Kappos 2006's public accessibility. Finally, HEC

says Novartis waived the right to dispute the issue in the pre-trial order. It did not. The Court should thus reject HEC's anticipation attack simply for lack of proof that Kappos 2006 is prior art.

If the Court reaches the question, Kappos 2006 is missing two claim elements. Kappos 2006 describes an upcoming Phase III trial in which the 0.5 mg daily dose would be *tested* for the very first time. The Patent, however, does not claim a test; it claims a *treatment*. As the Court found in the PI, "Kappos 2006 was a test. It was a hypothesis. It does not disclose and does not anticipate the treatment limitations of the asserted claims of the '405 patent." (D.I. 583 at 4.) No evidence HEC offered at trial should change that conclusion. In addition, Kappos 2006 does not disclose to a person of skill that a loading dose was necessarily excluded from the clinical trial design. Finally, Kappos 2006 is not enabling for a person of skill to use 0.5 mg to treat patients before the patent was filed, and as such it cannot anticipate. Because HEC cannot carry its clear and convincing evidentiary burden, and for other reasons explained below, the Court should uphold the 405 Patent.

FACTS

The Court heard live testimony from six expert witnesses and video testimony from five fact witnesses during the March 2–5, 2020 trial. (*See* NFOF 82–102.)

Inventors Hiestand and Schnell used a new approach to the well-accepted EAE animal model of MS to discover that unexpectedly low doses of fingolimod could be used to treat RRMS. Their experiment used a casting technique to study blood vessel growth and showed that a dose as low as 0.3 mg/kg once per week completely eliminated EAE relapses in rats. That weekly dose converts to a daily dose of 0.042 mg/kg (0.3 divided by 7), far lower than the lowest daily dose in the prior art of 0.1 mg/kg daily. A person of skill would understand that dose in turn to translate to the 0.5 mg human dose disclosed in the human example of the patent. (NFOF 125–28.)

Novartis filed a patent application in Great Britain on June 27, 2006 including these EAE results and a corresponding prophetic human example illustrating and expressly reciting the use of a 0.5 mg daily dose of fingolimod to treat RRMS patients. Specifically, the human example stated "patients with relapsing-remitting MS receive [fingolimod] at a daily dosage of 0.5 . . . mg" for "treatment" of their condition, begun "initially" at the start of therapy. (NFOF 66–75.)

The identical application was re-filed in the U.S. patent system, leading to the 405 Patent with six claims. Claim 1 is directed to "a method for reducing or preventing or alleviating relapses in [RRMS] in a subject in need thereof, comprising orally administering to a subject [fingolimod] . . . at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen." Claim 3 recites the same method for "treating" RRMS, and Claim 5 recites "slowing progression" of RRMS. Dependent claims 2, 4, and 6 each specify fingolimod hydrochloride. (NFOF 67, 77.)

In 2017, generic drug makers challenged the Patent in an IPR on three grounds—two obviousness arguments, and one anticipation argument based on an underlying written description attack. The PTAB rejected all grounds, and upheld the Patent in July 2018. (NFOF 78–80.) Within days, Novartis asserted the 405 Patent against 23 generic drug makers in this Court. (D.I. 1 ¶ 223, Ex. B.) When several refused to commit not to launch their products at risk in August 2019, Novartis sought a PI. (D.I. 358.) After a live evidentiary hearing, the Court granted the motion, finding, among other things, that defendants were unlikely to carry their burden to prove the Patent invalid by clear and convincing evidence. (D.I. 583.) Defendants argued that Kappos 2006 anticipated the Patent, and that the specification lacked written description to support either the treatment purpose of the 0.5 mg daily dose or the absence of a loading dose—the same arguments HEC presented at trial. The Court found each of these challenges unlikely to succeed,

including because defendants had failed to present the testimony of a full person of skill in support of their arguments. *(Id.* at 4.)

During claim construction and the PI process, the Court adopted claim constructions and a person of skill definition that the parties do not dispute here (*see* D.I. 561, 563, 583):

- The Court construed the claim preambles to be "limiting statements of purpose," *i.e.*, to require that the method be practiced for the treatment purpose stated in the preamble—the same interpretation the PTAB had in the IPR. (*Id.*) The Court did not find that the preambles further require efficacy, although in the PI the Court accepted testimony that knowledge of efficacy would affect whether a doctor would administer fingolimod for the claimed purpose of treating RRMS. (D.I. 561 at 9; D.I. 583 at 4.)
- The Court adopted the PTAB's definition of a person of skill from the IPR: "a multi-disciplinary research team including 1) a Ph.D. with expertise in the area of neurology and/or an M.D. having several years of clinical experience treating multiple sclerosis patients, and who would be knowledgeable about the multiple sclerosis medical literature, and 2) a pharmacologist with experience in drug development." (IPR FWD at 11; D.I. 583 at 3.)

At trial, HEC challenged the Patent on written description and anticipation grounds only. While the pre-trial order also asserted obviousness and non-enablement, HEC abandoned those theories. (NFOF 103.) HEC's case came in primarily through three expert witnesses: Dr. Fujinami testified about EAE models; Dr. Savic provided the perspective of a pharmacologist; and Dr. Hoffman provided the perspective of an MS physician. The Court rejected HEC's effort to have Dr. Hoffman additionally qualified as an expert in clinical trials and their design. For that reason,

Dr. Hoffman declined to testify on direct regarding (and was not asked about on cross) the human example in the Patent. (NFOF 102, 109.)

Novartis's rebuttal case came in primarily through its three experts: Dr. Fred Lublin, an MS physician and clinical trial specialist personally involved in fingolimod's clinical trials; Dr. Lawrence Steinman, an MS physician, EAE specialist, and pioneer in developing other MS therapies; and Dr. William Jusko, a highly decorated pharmacologist specializing in immunosuppressants, with extensive direct experience with fingolimod reflected in some prior art publications. (NFOF 90–99.)

The totality of the evidence at trial showed—consistent with the PTAB's ruling and this Court's PI ruling—that HEC failed to prove by clear and convincing evidence that the Patent specification did not support the claims. In addition, HEC failed to show that the putative anticipation reference Kappos 2006 was prior art, or that it anticipated the Patent.

ARGUMENT

HEC agrees that the Patent is presumed valid, and that the burden to prove invalidity is by clear and convincing evidence. (HCOL 6, 7.) HEC conceded that this burden requires more than equal but opposing expert views. (Tr. 978:24–980:1.) HEC has failed to carry its burden.

Spotlighting its failures at trial, HEC starts its brief by attempting to introduce new evidence. HEC pastes in a portion of an internal Novartis email from the PI (at 3), and cites an unofficial, HEC-made transcript of the Federal Circuit argument in the IPR appeal (at 4). These documents are outside of the trial record and are irrelevant—HEC offers no basis for the Court to consider these materials, and there is none. The Novartis email was never listed as a trial exhibit (*see* PTO Exs. 10–12, *passim*), was never introduced at trial, and lacks any evidentiary foundation or explanation. The "transcript" is likewise inadmissible—it is not an official document subject

to a hearsay exception, FED. R. EVID. 803, and it concerns an IPR trial record different than the record in this case. Plus, the appeal has been dismissed, making the colloquy at oral argument even more beside the point.

HEC also complains (at 3) that Novartis allegedly delayed in asserting the 405 Patent. This argument is beside the point, having nothing to do with written description or anticipation. It is also wrong. Novartis asserted the Patent immediately after the IPR final decision upholding the claims. (D.I. 1 ¶ 223, Ex. B.) This Court forcefully rejected the point during the PI proceedings (D.I. 583 at 8), and HEC gives no reason why anything is different now.

Turning to arguments that are relevant, HEC's proof at trial fell far short of what is needed.

I. The Patent Provides Written Description Under 35 U.S.C. 112

Written description turns on "whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Id*.

Despite *Ariad*'s admonition to focus on "the four corners of the specification from the perspective of a person of ordinary skill in the art," HEC starts with a digression into the Patent's prosecution history. HEC complains (at 1–2) that Novartis altered the claims that accompanied the application when it was filed initially. If anything, the extensive prosecution history strengthens written description, contrary to HEC's arguments.

A foundational basis for the presumption of validity is the belief that patent examiners will do their jobs during examination. *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 97 (2011)

(observing presumption of validity's grounding in "'the basic proposition that a government agency such as the [PTO] was presumed to do its job'") (*quoting American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F. 2d 1350, 1359 (Fed. Cir. 1984)). That presumption was amply borne out in the prosecution record here, with multiple iterations of communications between the Patent Office and Novartis evidencing a rigorous review—including review for compliance with the Patent Laws' written description requirements. *See, e.g.*, MPEP § 2163. HEC's effort to use innuendo to impugn the Examiner's work is wildly off the mark. The mere fact that the claims changed during prosecution is routine, not evidence of sloppiness by the Patent Office, and HEC cannot show otherwise. (NCOL 45 (citing *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 622, 683 (Fed. Cir. 2000), *vacated on other grounds*, 535 U.S. 722 (2002); *Application of Johnson*, 558 F.2d 1008, 1019 (C.C.P.A. 1977); 37 C.F.R. § 1.121(c))).

A. The Specification Supports the Treatment Purpose of the 0.5 mg Dose

When it finally turns to the specification itself, HEC attacks the written description for the 0.5 mg dose piecemeal, separately criticizing the EAE example and the human example. (*See* HEC. Br. at 16–27.) That approach is misguided. The specification must be read as a whole.[1]

As Novartis's experts showed at trial, the different parts of the specification work together. The entire specification emphasizes that the invention is about the use of S1P receptor agonists, in particular fingolimod, for the treatment of MS, including reducing relapses and slowing

[1] *See Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1346 (Fed. Cir. 2000) ("Compliance . . . with the written description requirement requires that . . . the [original] specification considered as a whole must convey to one of ordinary skill in the art, either explicitly or inherently, that [the inventor] invented the subject matter claimed . . . ."); *In re Tropp*, 748 F. App'x 1022, 1024 (Fed. Cir. 2018) (vacating and remanding written description decision where Board "did not consider the *entire* . . . specification in assessing whether there was sufficient written description support"); *In re Wright*, 866 F.2d 422, 425 (Fed. Cir. 1989) ("In deciding the issue, the specification as a whole must be considered.").

progression in RRMS. (NFOF 69–70, 111; JTX-001 at 1:1–10:31.) The specification then provides two examples—a synopsis of the inventors' work using the EAE model of MS, and a prophetic human example using specific doses of fingolimod. (NFOF 71–75, 112; JTX-001 at 10:32–11:19.) The EAE example reports results that show a dose as low as 0.3 mg/kg once per week is effective in rats, a far lower drug exposure than any prior report. (NFOF 73, 125; JTX-001 at 10:21–11:2.)

That result then informed the human treatment example, which expressly identifies a lower dose than had been used in RRMS patients before, 0.5 mg daily. (NFOF 74–75; JTX-001 at 11:3–19.) Specifically, the human example recites that "patients with relapsing-remitting MS receive [fingolimod] at a daily dosage of 0.5 . . . mg [orally]" as a "treatment." (JTX-001 at 11:8–16.) Although the application was re-filed a number of times internationally and in the United States, the content of the specification never changed. (NFOF 66.) The Patent Office ultimately issued claims that track exactly what the human example describes.

None of HEC's witnesses analyzed the Patent from a holistic perspective, nor could they. Dr. Hoffman declined to testify about the human example altogether, due to lack of clinical trial expertise. (NFOF 102, 109.) Neither Dr. Fujinami nor Dr. Savic is a clinician. (NFOF 100–01.) HEC thus failed to provide testimony about the specification as a whole from the perspective of a full person of skill (which includes an M.D.). That is reason enough to find that HEC has failed to deliver clear and convincing evidence[2]—a similar error to what Chief Judge Stark found in the

[2] *See Wyeth Holdings Corp. v. Sandoz, Inc.*, 2012 WL 1748008, at *13 (D. Del. Apr. 5, 2012) ("In the absence of any evidence from an expert or person of skill in the art, and given the conflicting evidence cited by Wyeth, Sandoz's bare argument does not rise to the level of clear and convincing evidence."); *M2M Sols LLC v. Sierra Wireless Am., Inc.*, 2016 WL 1298961, at *3 (D. Del. Mar. 31, 2016) ("[C]onclusory arguments, unsupported by expert opinion about what a person of skill in the art would understand and directly contradicted by considerable expert

PI, where defendants had failed to provide testimony from the other half of the person of skill, a pharmacologist. (D.I. 583 at 6.) In any event, HEC's criticisms of the specification's constituent elements are without foundation. Each provides more than enough written description to support the claims.

1. The Prophetic Human Example Specifically Recites a 0.5 mg Daily Dose for Treatment of RRMS

The human example describes an "[i]nvestigation of clinical benefit" in which "20 patients with relapsing-remitting MS receive [fingolimod] at a daily dosage of 0.5 . . . mg" and are evaluated on a regular basis for "[d]isease state and change in disease progression." (JTX-001 at 11:4–13.) Patients "initially" receive "treatment for 2 to 6 months," and thereafter "remain on treatment for as long as their disease does not progress and the drug is satisfactorily tolerated." (*Id.* at 11:14–16.) Earlier, the specification identifies treatment embodiments including methods for reducing or preventing or alleviating relapses or slowing progression of MS. (*Id*. at 9:32–33, 9:40–41.) The human example thus matches the claims exactly—claims 1 and 2 are to a method for using 0.5 mg daily to reduce, prevent, or alleviate relapses in RRMS patients; claims 3 and 4 are to using the method to treat the disease generally; and claims 5 and 6 are to slowing the disease's progression. (*Id.* at 12:49–13:9.)

At trial, HEC repeatedly attacked the human example as "fake" (*see* Tr. 85:20–86:6, 99:14–18, 242:12), but now concedes that such prophetic or "paper" examples can be proper written description support (HEC Br. 25).[3] Unable to avoid the human example, HEC first contends (at

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testimony, do not meet Defendants' considerable burden of establishing invalidity for lack of written description by clear and convincing evidence.").

[3] *See also Ariad*, 598 F.3d at 1357 ("Prophetic examples are routinely used in the chemical arts, and they certainly can be sufficient to satisfy the written description requirement."); *Hoffmann-La Roche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1377 (Fed. Cir. 2003) ("[Paper] examples have long

21, 25, 27) that the example lacks a "descriptive link" to the actual data from the EAE example. No such requirement exists. To the extent the law demands a "descriptive link," the "link" refers to the connection between a prophetic example and the claims, not a prophetic example and another example in the patent.[4] The specification provides just such a link between the human example and the claims—the claim language is almost word-for-word what is in the human example. Even if a "descriptive link" was somehow required between two examples, Drs. Steinman and Jusko showed that a person of skill would understand the link between the EAE and human examples, as discussed below in Section I.A.3.

HEC also argues that the human example was "never run nor intended to be, and so it 'is not so much an example as it is a mere mention of a desired outcome.'" (HEC Br. 27 (quoting *CreAgri, Inc. v. Pinnaclife, Inc.*, 2013 WL 6673676, at *12–13 (N.D. Cal. Dec. 18, 2013), *aff'd*, 579 F. App'x 1003 (Fed. Cir. 2014)); *see also id.* at 25.) This is nonsensical. As drafted, prophetic or paper examples are not actually run—that is what makes them prophetic.[5] Furthermore, here, unlike in *CreAgri* and other cases HEC cites (at 25–27), the prophetic example does not stand

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been accepted in patent documents . . . . The patent law authorizes that an invention may be constructively reduced to practice by filing a patent application, whether the embodiments were actually made or are constructed in the patent application.").

[4] *See, e.g.*, *Bone Care Int'l, L.L.C. v. Roxane Labs., Inc.*, No. 09-CV-285 GMS, 2012 WL 2126896, at *35 (D. Del. June 11, 2012) ("prophetic . . . examples 'can be sufficient to satisfy the written description requirement,' if the disclosure has a 'descriptive link' *to the claimed invention*") (quoting *Ariad*, 598 F.3d at 1357) (emphasis added).

[5] *See* MPEP § 2164.02 ("An example may be 'working' or 'prophetic.' . . . A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved."); *Hoffmann-La Roche*, 323 F.3d at 1374 n.2 ("Paper examples describe the manner and process of making an embodiment of the invention which has not actually been conducted.").

alone in the specification. It is a logical extension of the EAE experiment, as Novartis's witnesses attested. (NFOF 110–12.)

More fundamentally, HEC points to no evidence that a person of skill would read the human example as "a mere mention of a desired outcome." (*Cf.* HEC Br. 25–27.) Dr. Savic never suggested that, and Dr. Hoffman declined to testify about the human example at all. In contrast, Drs. Lublin, Steinman, and Jusko all explained that a person of skill would understand the human example to illustrate the invention in action as a "treatment." (NFOF 104–09.) Without testimony from an M.D.—and in the face of considerable physician expert testimony to the contrary—HEC cannot satisfy its heavy burden of proving invalidity for lack of written description by clear and convincing evidence. The proof on this is entirely one-sided, and disposes of HEC's argument.

HEC next urges (at 26) that the human example is "not directed to assessing treatment of the claimed disease," RRMS, because it "assesses disease *progression*" and does not "discuss *relapses or remissions*." This idea flies in the face of what the example says—the very first line states that it is about "patients with relapsing-remitting MS[.]" (JTX-001 at 11:8.) That is the "claimed disease." The example also says that the patients receive "treatment" (*id.* at 11:14–16), which is the whole subject of the Patent; the specification recites in particular "reducing or preventing or alleviating relapses" and "slowing progression of . . . disease" as embodiments of such treatment, tracking the language of the claims. (*Id*. at 9:32–33, 9:40–41.) The PTAB found, and Drs. Lublin, Steinman, and Hoffman all testified, that "treatment of RRMS" includes reducing relapses as well as slowing disease progression. (IPR FWD at 14 ("We further construed the terms 'reducing or preventing or alleviating relapses' and 'slowing progression' as subsumed within the genus of 'treating' RR-MS."); NFOF 77.)

Once again, the record is devoid of any actual evidence to support HEC's notion. No witness ever suggested at trial that the example was about some other form of MS. Indeed, HEC's unsupported assertion (at 26) that the "study focuses ['not on RRMS' but] on the differing progressive forms of MS" where "the disease begins to progress" has it backwards: the example discloses that the treatment *stops* if the disease progresses. (JTX-001 at 11:14–16 ("Thereafter, they remain on treatment for as long as their disease does not progress and the drug is satisfactorily tolerated.").) HEC's new argument has no basis in the evidence.

HEC lastly criticizes various other aspects of the human example that essentially amount to an argument that it did not rise to the level of an actual FDA-approved clinical trial: that "efficacy, or clinical outcome, are not even mentioned," that the sample size was small, that there is no "statistical measure of results or even raw results," and that the prophetic trial "would not have met the requirements for a Phase III clinical study." (HEC Br. 26–27.) These critiques are irrelevant in the context of a patent application. Clinical trial data are not required in a patent.[6]

Nor is the purpose of the 405 Patent's human example to mimic an FDA-approved trial. Instead, as Dr. Steinman explained, the example tells a person of skill how to administer the dose and "how you would follow the patient on that dose to understand whether clinical benefit was being achieved," in other words, an "[i]nvestigation of clinical benefit" as the example states. (Tr. 733:25–736:3.) Or, as Dr. Lublin explained (Tr. 237:25–239:1), the human example is the invention in action.

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[6] *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1324 (Fed. Cir. 2009) ("[H]uman trials are not required for a therapeutic invention to be patentable."); *Scott v. Finney*, 34 F.3d 1058, 1063 (Fed. Cir. 1994) ("Testing for the full safety and effectiveness of [the invention] is more properly left to the Food and Drug Administration (FDA)."); MPEP § 2164.05 ("[C]onsiderations made by the FDA for approving clinical trials are different from those made by the USPTO in determining whether a claim is enabled.").

2. The EAE Example Describes the Inventors' Experiment

HEC next contends (at 17–18) that a person of skill would think the EAE example lacks sufficient experimental details and data to show that the claimed treatment method works. HEC is wrong, but also off-point.

As the Federal Circuit has repeatedly held, written description does not require any experimental data at all, even for method of treatment claims.[7] Paper or prophetic examples that have not been performed have no data, yet they are still recognized as fully supportive of written description. Written description is an inquiry about "whether the skilled reader of the patent disclosure can recognize that what was claimed corresponds to what was described . . . not about whether the patentee has proven to the skilled reader that the invention works, or how to make it work, which is an enablement issue." *Centrak, Inc. v. Sonitor Techs., Inc.*, 915 F.3d 1360, 1366 (Fed. Cir. 2019) (quoting *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1191 (Fed. Cir. 2014)).

HEC's entire criticism of the EAE example is thus off base. While data may be needed in some cases to show enablement or utility, HEC has not pursued those challenges at trial. (NFOF 103.) The absence of what HEC considers sufficient data is thus a "legal irrelevanc[y]"—as this Court found in the PI. (D.I. 583 at 6.)

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[7] *Nuvo Pharm. (Ireland) Designated Activity Co. v. Dr. Reddy's Labs. Inc.*, 923 F.3d 1368, 1380 (Fed. Cir. 2019) ("our [written description] case law does not require experimental data demonstrating effectiveness") (citing *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1309 (Fed. Cir. 2015); *'318 Patent Infringement Litig.*, 583 F.3d at 1324; *see also Pfizer Inc. v. Teva Pharm. U.S.A., Inc.*, 882 F. Supp. 2d 643, 704 (D. Del. 2012), *aff'd sub nom. Pfizer Inc. v. Teva Pharm. USA, Inc.*, 555 F. App'x 961 (Fed. Cir. 2014) ("[B]ecause written description does not require reduction to practice," inventors need not "collect biological data" or "report such test results in the application.").

If data were required, the EAE example provides more than enough. It recites how the inventors injected Lewis rats with proteins to induce a relapsing disease that mimics RRMS. (JTX-001 at 10:32–40; NFOF 72–73, 113.) The rats then received different doses of "Compound A" (fingolimod), which the Patent reports "fully blocks disease-associated angiogenesis" and "completely inhibits the relapses phases" in the rats at several dosages, including dosages as low as 0.3 mg/kg administered once a week. (JTX-001 at 10:61–11:2; NFOF 72–73.) EAE was a well-established animal model of MS as of June 2006. (NFOF 38–42.) As Dr. Steinman explained, when read by a person of skill "in the context of the state of knowledge at the time of the invention" (*Zoltek Corp. v. United States*, 815 F.3d 1302, 1308 (Fed. Cir. 2016) (citation omitted)), the EAE experiment fully supports the claimed effect in RRMS, including by showing that "a dose lower than anyone had ever seen" could be used to treat RRMS. (NFOF 110–32.)

HEC complains (at 16–17) that the EAE experiment fails to disclose if the rats underwent relapses, or a single attack. Not true—the title of the example is "relapsing" EAE (JTX-001 at 10:32–33) and the specification says the data showed "results in . . . a relapse at around day 26" (*id*. at 10:38–40). Even HEC's own witness Dr. Hoffman testified that a person of skill would understand the example to describe "a relapsing rat model." (Tr. 625:12–626:4.) HEC cannot disregard what the specification says and evidence offered at trial.

HEC's stubborn denial of the specification's actual language is based on Dr. Fujinami's historical view that a person of skill "would understand that the Lewis rat model generally produces a monophasic disease," where the rat does not relapse. (HEC Br. 17 (citing HFOF 28).) That Lewis rats "generally produce" a monophasic disease does not preclude a relapsing version, and thus does not give license to disregard what the Patent says. In any event, Dr. Fujinami

admitted that the last time he worked with Lewis rats was 35 years ago, and that he last published a paper on Lewis rats in 1978. (NFOF 119.)

Dr. Hoffman acknowledged that, in more recent times, relapsing Lewis rats models have appeared in peer-reviewed publications, including in the Rausch 2004 paper co-authored by inventor Peter Hiestand. (NFOF 117–18.) Thus, Dr. Fujinami's information was simply out of date, as Dr. Steinman confirmed—he testified that Lewis rats are a "perfectly good model" for relapsing MS, pointing to the Rausch 2004 paper as an example. (NFOF 118.)

Again relying on the testimony of Dr. Fujinami, HEC further argues (at 17–19) that the specification does not disclose sufficient details about how the experiment was conducted, or "results sufficient" to support the Patent's conclusion that fingolimod "fully blocks disease-associated angiogenesis and completely inhibits the relapse phase when administered daily" (JTX-001 at 10:64–11:2). This argument amounts to an allegation that the Patent is misrepresenting the truth. But other than Dr. Fujinami's conclusory statements, HEC has presented no evidence of that. Dr. Steinman explained that none of Dr. Fujinami's criticisms would cause a person of skill to doubt the results of the experiment. (Tr. 781:9–782:18.)

HEC argues (at 15–16) that Novartis's evidence merely shows that the invention would have been obvious, because the human example and the EAE example "contain gaps that a [person of skill] can only fill by tu[r]ning to a panoply of prior art references." As shown above, the examples contain no "gaps" that need filling. To the extent Novartis's experts referred to art, this is appropriate; "[t]he [written description] requirement is applied in the context of the state of knowledge at the time of the invention." *Zoltek*, 815 F.3d at 1308; *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005); *MorphoSys AG v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354, 364 (D. Del. 2019). HEC's main case on this point (at 15–16), *L.A. Biomedical*

Research Inst. at Harbor-UCLA Med. Ctr. v. Eli Lilly & Co., 849 F.3d 1049 (Fed. Cir. 2017), is inapposite. The priority application in that case did not disclose the claimed dose at all. *Id.* at 1057. As a result, a person of skill had to make assumptions based on the prior art—including at least one as to which the patentee presented no evidence—to arrive at that dose. *Id.* at 1058. Here, the 0.5 mg dose is explicitly disclosed in the human example. No "assumptions" were needed.

HEC's experts were simply unable to or chose not to read the Patent from the perspective of a person of skill. Dr. Fujinami's EAE knowledge was outdated (*see infra* at 16–17), and Dr. Savic deliberately assumed that a person of skill would be ignorant of certain prior art references when reading the Patent (Tr. 508:14–509:8), contrary to black letter law. *LizardTech*, 424 F.3d at 1345 ("[T]he patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before."); *Zoltek*, 815 F.3d at 1308; *see also MorphoSys*, 358 F. Supp. 3d at 364. Their opinions thus cannot help HEC.

3. The EAE Example Supports the 0.5 mg Human Dose

HEC's final major complaint (at 20–21) is that the Patent does not describe how to translate the EAE animal results into human doses. It did not have to—the 0.5 mg daily dose was already spelled out in the human example, and a person of skill would appreciate the connection anyway, as Drs. Steinman and Jusko testified. (NFOF 125–32.)

This Court rejected similar arguments at the PI stage, when it held that "[a] patent does not need to tell the full story or really even any story about how the inventors came to their invention, and it need not state things that a POSA would already know, including the prior art." D.I. 583 at 6; *see also Nuvo*, 923 F.3d at 1380 (citing *Allergan*, 796 F.3d at 1309) (written description "does not require theory or explanation of how or why a claimed composition will be effective"); *Zoltek*, 815 F.3d at 1308 ("The written description 'need not include information that is already known and available to the experienced public.'") (quoting *Space Sys./Loral, Inc. v. Lockheed Martin*

Corp., 405 F.3d 985, 987 (Fed. Cir. 2005)). Here, the Patent includes an animal example showing that a much lower dose of fingolimod could inhibit relapses, and a human example specifically identifying a new lower dose in humans, 0.5 mg daily. The law requires nothing more.

HEC's pharmacologist Dr. Savic complained that the Patent does not say how the inventors translated the rat to the human dose. (HFOF 42, 45.) Dr. Jusko showed why Dr. Savic was mistaken. Her analysis was based on models used to translate animal to human doses for first-in-human use. (NFOF 129.) But by June 2006, fingolimod had already been used in humans for years, in clinical trials in renal transplant patients and in RRMS. The correlation between fingolimod's efficacy in animals and humans was already established. (*Id.*) In that context, the proportional relationship between the lowest EAE rat and human doses in the specification would be very logical. (NFOF 127.)

HEC quibbles that the inventors' actual proportionality analysis differed from how Drs. Steinman and Jusko say a person of skill would understand the Patent. This is irrelevant. What matters is whether the "four corners of the specification," read in view of "the existing knowledge in the particular field [and] the extent and content of the prior art," "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter." *Ariad*, 598 F.3d at 1351. The differences between the inventors' and a person of skill's analyses merely show that different proportional relationships lead to the same place—further corroborating the reasonableness of the link between the EAE and human studies in the Patent.

B. The Patent Specification Describes the Limitation "Absent an Immediately Preceding Loading Dose Regimen"

The claims' exclusion of a loading dose was introduced during prosecution in response to an Examiner's rejection. The PTAB has already rejected the theory that the specification lacks support for the absence of a loading dose, under an evidentiary standard far more favorable to the

Patent challenger than the one here. As the Federal Circuit has explained, "it may be harder to meet the clear and convincing burden when the invalidity contention is based upon the same argument on the same reference that the PTO already considered." *Sciele Pharma Inc. v. Lupin Ltd.*, 684 F.3d 1253, 1260–61 (Fed. Cir. 2012).[8] That makes sense in view of the foundational reason for the presumption of validity, *i.e.*, the belief that the Patent Office will do its job during prosecution and review. *See i4i*, 131 S.Ct. at 2243.

In the IPR, the petitioners argued that this same supposed lack of written description deprived the Patent of the June 2006 priority date, and thus rendered the Patent anticipated by a 2010 reference. (IPR FWD at 40–45.) Petitioners in the IPR had to prove their case only by a preponderance of the evidence. (*Id.* at 45.) They could not do so. The PTAB considered "the record as a whole" and found that Novartis had "demonstrated that the claims of the '405 patent are supported" by the human example in the specification. (*Id.*) The evidence showed "absence of an immediately preceding loading dose regimen" was fully described by the patent. (*Id.*) The PTAB found Drs. Jusko and Steinman "credible" and "well-qualified to testify as to the understanding of one of ordinary skill in the relevant art" with respect to this issue. (*Id*. at 44.) This Court agreed in the PI. (D.I. 583 at 5–6.)

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[8] *See also Endo Pharm. Inc. v. Mylan Pharm. Inc.*, No. 11-CV-00717 (RMB/KW), 2014 WL 334178, at *6 (D. Del. Jan. 28, 2014), *motion for relief from judgment granted*, No. 11-CV-717 (RMB/KW), 2014 WL 2532179 (D. Del. June 2, 2014) ("Although Defendants' burden does not change, evidence considered by the PTO may not be given the same weight as new evidence.") (citing *Sciele*, 684 F.3d at 1260); *Cubist Pharm., Inc. v. Hospira, Inc.*, 75 F. Supp. 3d 641, 659 (D. Del. 2014), *aff'd*, 805 F.3d 1112 (Fed. Cir. 2015) ("Practically speaking, however, 'it may be harder to meet the clear and convincing burden when the invalidity contention is based upon the same argument on the same reference that the PTO already considered.'") (quoting *Sciele*, 684 F.3d at 1260–61).

HEC contends these decisions were wrong. But HEC concedes or does not dispute that written description is a question of fact (HCOL 65); that the issue is evaluated from the perspective of a person of skill (HCOL 63); that Novartis provided testimony from that perspective via Drs. Jusko and Steinman in the IPR and again at trial; and that Novartis's experts found written description for the loading dose exclusion. HEC further failed to provide contrary testimony from a full person of skill—as discussed above (at 6–7, 10–11), HEC's physician witness did not testify about the human example at all. In these circumstances, HEC cannot possibly carry the clear and convincing burden that applies here.

HEC chose not to participate in the IPR, but apparently hoped the Federal Circuit would reverse the IPR decision (*See* HEC Br. 4; D.I. 749). Instead, the Federal Circuit dismissed the appeal for lack of jurisdiction and rendered no merits opinion. *Argentum*, 2020 WL 1944759. HEC's only other argument is that the specification can be found insufficient as a matter of law, without testimony on how a person of skill would read the specification. HEC is wrong. The record at trial only bolstered the correctness of the IPR decision.

1. Written Description of a Negative Claim Limitation Is Governed by the Same Standard as Any Other Limitation

On the law, HEC contends (at 5–8) that under *Santarus*, 694 F.3d at 1351, the specification must include a "reason to exclude the relevant limitation" to provide adequate written description. That is incorrect. The Federal Circuit has squarely held that "*Santarus* did not create a heightened standard for written description support of negative limitations." *Nike, Inc. v. Adidas AG*, 812 F.3d 1326, 1348 (Fed. Cir. 2016), *overruled on other grounds by Aqua Products, Inc. v. Matal*, 872 F.3d 1290 (Fed. Cir. 2017). Instead, the standard is the same as for any other limitation: "whether the disclosure of the application relied upon reasonably conveys to those skilled in the

art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351.

Santarus at most says that a "reason to exclude" in the specification can be one way to support a negative limitation, but it does not hold it is the only way. The *Santarus* court credited the patentee's expert's view that the specification provided a reason to exclude the limitation at issue, so the court never had to address other ways to provide written description. *Id.* at 1351. The Court in *Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1356 (Fed. Cir. 2015), later confirmed that "[w]hen viewed in its proper context, *Santarus* simply reflects the fact that the specification need only satisfy the requirements of § 112, paragraph 1 as described in this court's existing jurisprudence[.]" Likewise, *Nike* confirmed that, when evaluating a negative limitation, "we need only consider . . . the customary standard for the written description requirement" when evaluating a negative limitation. 812 F.3d at 1348. That "customary standard" does not include any analysis of whether there is a reason to exclude. Thus, the *Nike* court never considered whether there was a reason to exclude. *Id.* at 1348–50.

HEC argues (at 7) that the "comprising" term in the claims here demands a reason to exclude. HEC cites no support for this idea. Neither MPEP § 2173.05(i) nor *Ex parte Grasselli*, 231 USPQ 393 (B.P.A.I. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984) cited by HEC mention comprising claims. On the contrary, the MPEP section actually cites *Grasselli* for the proposition that "[i]f alternative elements are positively recited in the specification, they may be explicitly excluded in the claims"—without mention of a reason to exclude.[9] Indeed, the same MPEP section

[9] In any event, the one paragraph on written description in *Grasselli* (a 1983 appeal from a Patent Office rejection) does not describe the arguments for or against written description for the negative claim limitation at issue, or whether there was expert testimony to support them. *See* 231 USPQ 393 at *2. The fact that in this particular case the Board agreed with the examiner that the negative

states that "a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a prima facie case for lack of descriptive support." MPEP § 2173.05(i) (citing *Ex parte Parks*, 30 USPQ 2d 1234, 1236 (B.P.A.I. 1993)).

Accordingly, the law provides no support for HEC's attack on the loading dose term in the specification. The facts do not either.

2. Under the Correct Standard, The Specification Supports the Loading Dose Term

HEC agrees (at 4) that a loading dose is a higher dose administered at the beginning of treatment. (*See also* NFOF 135.) But the Patent describes administering a "daily dosage of 0.5 . . . mg" fingolimod to treat RRMS, given "initially." (JTX-001 at 12:8–13.) The specification's statement that "[i]nitially, patients receive treatment," *i.e.*, "a daily dosage of . . . 0.5 mg[,]" emphasizes the absence of a loading dose. If a loading dose were directed, the Patent would say that a loading dose should be administered "initially." (NFOF 134.) As Dr. Steinman testified, "by starting out with a daily dose," the specification "necessarily preclude[s] a loading dose." (Tr. 766:7–15.) Dr. Hoffman agreed a loading dose would usually be given "as the first dose," *i.e.*, what would be given initially. (Tr. 547:12–548:1.) There is no room for a loading dose in this regimen.

HEC never addresses the specification's use of "daily" and "initially," much less the broader context of the entire specification. HEC instead maintains (at 7–8) that the absence of the words "loading dose" in the specification is fatal. But it has long been the law that "the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at

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claim limitation was not supported says nothing about the legal requirements for support of such limitations.

issue." *Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1376 (Fed. Cir. 2002); *see also Application of Smith*, 481 F.2d 910, 914 (C.C.P.A. 1973) (same). Instead, "one skilled in the art, reading the original disclosure, must reasonably discern the limitation at issue in the claims." *Crown Operations*, 289 F.3d at 1376; *see also All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774, 779 (Fed. Cir. 2002) ("[T]he failure of the specification to specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented.").

Contrary to HEC's suggestion (at 10–12), courts routinely rely on expert testimony about how a person of skill would understand a specification. "The [written description] requirement is applied in the context of the state of knowledge at the time of the invention," *Zoltek*, 815 F.3d at 1308, and expert testimony is often needed to explain that context. For example, in *Bone Care*, the court relied heavily on expert testimony about why certain claim elements were disclosed by a prophetic example, even though the example did not explicitly disclose those elements. *See* 2012 WL 2126896 at *37–39. HEC's cases are not to the contrary.[10] Even in *Santarus*, the Federal Circuit relied on expert testimony about how a person of skill would understand the specification. *See* 694 F.3d at 1351; *see also Nike*, 812 F.3d at 1359 (relying on expert testimony about how person of skill would understand patent figures to conclude that specification supported claims). That is exactly the kind of testimony Novartis relies on here.

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[10] Each of *Nuvo*, 923 F.3d at 1381 n.4; *Univ. Of Rochester v. G.C. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004); *PIN/NIP, Inc. v. Platte Chem. Co.*, 304 F.3d 1235, 1247–48 (Fed. Cir. 2002); and *Hyatt v. Boone*, 146 F.3d 1348, 1353 (Fed. Cir. 1998), hold only that experts must focus on the specification's language, and absent a genuine fact dispute, judgment as a matter of law on written description is possible. In each case, no fact dispute existed between the experts. That is the opposite of the record here.

HEC implies (at 8) that the prosecution history somehow impugns the loading dose term. As discussed above (at 8), the specification, not the prosecution history, provides written description. But in any event, the file history here shows Novartis excluded a loading dose as a routine response to an examiner's question about another reference. (JTX-064.0064, 0143–0147, 0207–208; NFOF 67–68.) As the partial concurrence in *Santarus* observed, "a negative limitation may be prudently placed in a claim in response to an examiner's rejection, perhaps to distinguish a reference that was given its 'broadest reasonable interpretation' for purposes of examination." *Santarus*, 694 F.3d at 1359 (Newman, J., concurring in part and dissenting in part). The examiner accepted Novartis's answer and granted the claims (JTX-064.0221), and that decision is entitled to deference here—the examiner is presumed to have done his job. *i4i*, 564 U.S. at 97. The specification backs up that presumption in fully supporting the exclusion of a loading dose. *See also Johnson*, 558 F.2d at 1019 (finding negative claim limitation supported when patentee amended claims to exclude two species of originally claimed genus, noting that "[a]ll that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count").[11]

HEC says (at 8) that Novartis's amendment would have been "superfluous" if "daily dosage" were enough to exclude an immediately preceding loading dose. Not so. It is the specification read as a whole—including its description of a "daily dosage of 0.5 [mg]" given

[11] HEC's argument (at 13–14) that Novartis argued during prosecution that the claims were not obvious "because the prior art taught a POSA to use loading doses for MS treatments" completely mischaracterizes the prosecution record. Novartis's statements about the reference at issue, Kovarik, were general. Kovarik was not directed to MS treatments, or even fingolimod specifically. It is hard to see how HEC got from Novartis's statements that "Kovarik is entirely about loading doses" and "Kovarik thus teaches away" to the notion that "the prior art taught a POSA to use loading doses for MS treatment." HEC's argument is meritless.

"initially" at the beginning of treatment—that supports the term. In isolation, the claims' recitation of a "daily dosage of 0.5 mg" does not reflect that full context, including the term "initially." Thus, Novartis's amendment was not "superfluous"—it merely clarified a point for the examiner.

HEC argues also (at 9) that if Kappos 2006 does not preclude a loading dose, the 405 Patent cannot either. HEC has it backwards: That HEC's experts testified that Kappos 2006 *does* exclude a loading dose is further support for the absence of a loading dose in the claims. As Novartis's experts showed, Kappos 2006 is a short abstract of an upcoming clinical trial. (NFOF 165.) That sort of document could not give a person of skill confidence that the full dosing regimen was necessarily provided. But the Patent is a fully-realized invention—a complete disclosure of the dosing regimen. (NFOF 138.) This Court agreed in the PI "that a POSA may well read an abstract differently than they read a patent." (D.I. 583 at 6.) Thus, if, as HEC's experts contend, a "daily dose" in an incomplete document like Kappos 2006 would preclude a loading dose—which Novartis disputes, as shown below (at Section II.B.2)—then that same reasoning would apply with even greater force to a complete disclosure like the Patent.[12]

HEC contends next (at 9) that Novartis's experts "made a series of admissions establishing that the specification's disclosure of a 0.5 mg daily dosage does not necessarily exclude a loading dose[.]" That badly mischaracterizes the testimony. Dr. Jusko said that he "could envision the possibility of starting with a loading dose" not about the specification's complete dosing regimen, as HEC implies, but with respect to fingolimod's pharmacology generally. (Tr. 897:14–898:10.)

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[12] HEC also confuses the standards for inherent anticipation and written description. Inherent anticipation requires that Kappos 2006 "necessarily" preclude a loading dose; written description requires that a person of skill read the specification to show "possession" of the invention. *Compare Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295 (Fed. Cir. 2002) (inherent anticipation), with *Ariad*, 598 F.3d at 1351 (written description).

Novartis's witnesses elsewhere provided unrebutted testimony that a person of skill would read the Patent as a complete description of the dosing regimen (unlike in Kappos 2006). (NFOF 138.) HEC says also (at 9) that Dr. Steinman admitted that "the specification has not [sic] textual hook for a loading dose." All Dr. Steinman actually said was that "you have the claims and you have the specification, which I understand doesn't change" and that "you couldn't put a textual hook into something that doesn't change." (Tr. 827:5–16.) But as discussed above (at 23), Dr. Steinman testified that the specification already contained at least two textual "hooks" for the loading dose exclusion: 1) a "daily dosage of 0.5 . . . mg" and 2) given "initially."

3. Even Under HEC's "Reason to Exclude" Standard, the Specification Fully Supports the Loading Dose Term

Even under the non-existent "reason to exclude" standard, a person of skill would have understood the 405 Patent specification to support the loading dose exclusion.

The specification describes the use of fingolimod to treat RRMS. All experts agreed that the use of a loading dose with fingolimod for RRMS would pose significant risks, including bradycardia. (NFOF 139–40.) Dr. Hoffman himself pointed to a person of skill's view about the risk of bradycardia as one reason why he read Kappos 2006 to preclude a loading dose—even though Kappos 2006 says nothing about bradycardia. (Tr. 549:3–550:22.) Nonetheless, HEC maintains (at 11–13) that the specification's silence about bradycardia means that side effect cannot be a reason to exclude. But a patent's "written description 'need not include information that is already known and available to the experienced public.'" *Zoltek*, 815 F.3d at 1308. As the expert testimony showed, fingolimod's bradycardia risks were well-known. (NFOF 140.) While fingolimod had been used with a loading dose in transplant patients, the risk-reward tradeoffs could be different for a less-acute condition like RRMS. (Tr. 548:4-549:21.)

Consequently, by disclosing the use of fingolimod to treat RRMS, the specification provided a reason to exclude a loading dose. The Patent Office found that these facts amply support the exclusion of a loading dose in the claims. (IPR FWD at 44–45 (finding the testimony of Drs. Jusko and Steinman regarding support for the loading dose exclusion, including testimony regarding the risk of bradycardia, "credible and substantially unrebutted").)

II. HEC Failed To Prove Kappos 2006 Was Even Prior Art, Much Less Anticipatory

HEC contends (at 28–40) that Kappos 2006 anticipated the Patent. But HEC has failed to show that Kappos 2006 was publicly accessible before the June 27, 2006 priority date. Even if it had been, Kappos 2006 described only an upcoming placebo-controlled test, not the claimed method of treatment; left open the possibility of a loading dose in the regimen, which the Patent excludes; and did not enable doctors to treat with the untested 0.5 mg dose. Each of these infirmities alone would defeat HEC's anticipation defense. HEC fails to overcome any of them.

A. HEC Failed to Provide Any Competent Evidence That Kappos 2006 Was Publicly Accessible Before June 27, 2006

HEC agrees (at 28) that Kappos 2006 must have been "publicly accessible" before the priority date to even be a candidate to anticipate. HEC's primary evidence of public accessibility was DTX-9, a version of Kappos 2006 attached to a declaration from an alleged British Library employee, Rupert Lee. But the Court excluded DTX-9 as inadmissible hearsay. (Tr. at 372:13–374:9.) HEC now wants to reargue that decision. It also claims that other evidence proves public accessibility, and that Novartis supposedly waived the right to contest the issue anyway.

1. As the Court Found at Trial, the British Library Declaration Is Inadmissible Hearsay

HEC's post-trial brief rehashes (at 28–30) the exact argument the Court rejected at trial—that DTX-9 fits in FRE 807's residual exception to the hearsay rule. HEC does not say why the Court should revisit this issue. Courts urged to "reopen what has been decided" must take

"appropriate steps so that the parties are not prejudiced by reliance on the prior ruling." *Williams v. Runyon*, 130 F.3d 568, 573 (3d Cir. 1997); *see also Roberts v. Ferman*, 826 F.3d 117, 126 (3d Cir. 2016) ("[W]hen a court [reconsiders its prior decision], it must explain on the record why it is doing so and 'take appropriate steps so that the parties are not prejudiced by reliance on the prior ruling.'") (quoting *Williams*, 130 F.3d at 573). The prejudice here to Novartis would be extreme if the Court were to revisit its trial decision. The Court excluded DTX-9 early in Day 2 of a four-day trial. Novartis relied on that ruling, including by not introducing evidence to rebut the declaration. Short of a new trial, that reliance cannot be unwound—and HEC does not purport to seek a new trial, nor would one be warranted. For this reason alone, HEC's FRE 807 argument should be rejected.

The argument is also wrong. The declaration lacks any "guarantees of trustworthiness," especially "after considering the totality of circumstances under which it was made and evidence, if any, corroborating the statement[.]" FED. R. EVID. 807(a)(1). "The Rule 807 residual hearsay exception is to be used only rarely, and in exceptional circumstances, and is meant to apply only when certain exceptional guarantees of trustworthiness exist and when high degrees of probativeness and necessity are present." *United States v. Wilson*, 281 F. App'x 96, 99 (3d Cir. 2008).

As at trial, HEC continues to point to the declaration's contents for evidence of trustworthiness. (*See* HEC Br. 28–29; HFOF 70–73.) But hearsay cannot be used to "guarantee" its own trustworthiness, as the Court observed. (Tr. 367:15–373:10; FED. R. EVID. 807 Note to 2019 Amendment ("[T]he focus for trustworthiness [in the residual exception to the inadmissibility of hearsay] is on circumstantial guarantees *surrounding the making of the statement* itself, as well as any *independent evidence* corroborating the statement.") (emphases added).) HEC points also

to testimony from a Novartis corporate witness who said he had no reason to doubt some of DTX-9's contents. (HEC Br. 29; HFOF 74.) But there is no evidence the witness had any personal knowledge of declaration—he just read it and personally knew of no reason to dispute it. That does not make it trustworthy under the Federal Rules of Evidence. (*See* NCOL 61–63.)

DTX-9 on its face raises more questions than it answers. The declaration says Kappos 2006 was available on June 22, 2006 in a "Reading Room." (DTX-9.00001.) But a sticker on the abstract's cover page connects June 22, 2006 only with a "Document Supply Centre." (DTX-9.00004.) The declaration fails to explain the relationship between the two (if any), raising the question of how or when Kappos 2006 reached each location. Nor is it clear what the declarant personally knows about British Library practices from 2006; on the contrary, he admits relying "*to some extent on information collated by*" an unidentified "*third party*." (DTX-9.00001 (emphasis added).) Novartis sought a deposition of the declarant to probe these issues in May 2019. (Tr. 365:16–17.) But HEC claimed not to control the witness, did not provide him for deposition, and did nothing to otherwise address Novartis's concerns. (Tr. 365:7–366:22.) That is the opposite of "trustworthy," and indeed would be reason to discount the declaration on the merits even if it were admissible—which it is not.[13]

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[13] HEC cites *Nichols Inst. Diagnostics, Inc. v. Scantibodies Clinical Lab., Inc.*, 195 F. App'x 947, 950–52 (Fed. Cir. 2006), as support for relying on the declaration. (HEC Br. 29–30.) But in *Nicholss Inst. Diagnostics*, the key facts were all undisputed, including that the "multiple copies of the abstract were distributed directly to multiple interested members of the relevant public", that the reference was "mailed to subscribers, including scientists, attendees of industry-related conferences, universities and libraries," and that "at least one library . . . received an original copy . . . and that such copy would have been available for public use" prior to the critical date. 195 F. App'x at 950–51. It was also "undisputed that at least one library . . . received an original copy . . . and that such copy would have been available for public use" prior to the critical date. *Id.* at 951 (internal quotations omitted). The availability for public use *is* disputed here, and there is no evidence of any direct distribution to members of the public prior to the critical date in this case. These are exactly the facts in dispute here. HEC also cites *Twentieth Century Fox Film Corp. v.*

2. No Other Evidence Shows That Kappos 2006 Was Publicly Available Before June 2006

HEC contends (at 32–33) that evidence besides DTX-9 shows Kappos 2006 was publicly accessible before June 27, 2006. But HEC identifies no one who claims to have had access to Kappos 2006 before June 27, 2006. Lacking that evidence, HEC argues (at 32) that two Kappos 2006 authors—Drs. Aradhye and Calabresi—supposedly testified that "Kappos was necessarily published in advance of" a May 2006 European Neurological Society (ENS) meeting. Drs. Aradhye and Calabresi said no such thing.

Dr. Aradhye said that the abstract was prepared "in anticipation" of, and thus "in the supplement of[,] the ENS for that meeting." (*See* Tr. 672:19–24.) That says nothing about when the supplement became available—before, at, or after the meeting. Dr. Calabresi agreed that abstracts were published in conjunction with the ENS meeting, but he could not "actually remember with this meeting when people would have first had access to it." (Tr. 441:22–442:6.) He "did not actually attend this meeting," so he did not know. (*Id.* 442:7–8.) This testimony falls far short of "clear and convincing" evidence of when Kappos 2006 was publicly available. As in *Norian Corp. v. Stryker Corp.*, 363 F.3d 1321, 1330 (Fed. Cir. 2004), the co-authors did not know "whether copies of the Abstract were actually available to hand out" at the meeting, precluding a finding of public accessibility. None of the cases HEC cites are to the contrary. (NCOL 97.)

HEC's contention (at 32) that Dr. Aradhye "testified that Kappos 2006 was an abstract for a poster that was presented at the ENS meeting" is also incorrect. Dr. Aradhye testified that a

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Dastar Corp., 2000 WL 35503105, at *3 (C.D. Cal. Jan. 4, 2000) (HEC Br. 29), but the declaration there was submitted in support of summary judgment, where FRCP 56(c)(4) expressly permits declaration testimony.

related poster was included in the ENS supplement, which provided "a time for a poster display" (Tr. 675:2–676:18). But HEC relies on the abstract, not a poster, and has not provided the poster to the Court. More importantly, this testimony provides no evidence of the types of facts courts consider when assessing whether a meeting poster was "publicly accessible," such as how many people would have had access to the poster; how long the poster would have been available for public viewing; whether viewers could take notes or pictures of the poster; and similar facts. (NCOL 53–56.)

3. Both Parties Confirmed in the Pre-Trial Order That HEC Had The Burden To Show Public Accessibility

Lastly, HEC contends (at 30–32) that Novartis waived the right to dispute Kappos 2006's public accessibility before trial. That is incorrect. Page 1 of Novartis's pre-trial statement of facts states that HEC has "the burden of proof that the asserted prior art references are actually prior art to the 405 Patent." (PTO Ex. 2 ¶ 5.) HEC ignores this plain statement, instead suggesting (at 31) that Novartis only challenged the public accessibility of a reference other than Kappos 2006. But Paragraph 5 says HEC would bear the burden of proof for *all* "asserted prior art references," plural. There can be no dispute that Kappos 2006 is an "asserted reference." Indeed, HEC's own pre-trial "Statement of Issues of Fact That Remain To Be Litigated" acknowledges that one "issue to be litigated" is whether "Kappos 2006 is prior art to the '405 patent." (PTO Ex. 3, ¶ 59.) Then at trial, HEC admitted Novartis has disputed Kappos 2006's status as prior art since at least May 2019. (Tr. 364:25–367:3, 373:13–374:9.) Finally, HEC ignores that Novartis lodged multiple objections to DTX-9 in the pre-trial order, including for hearsay. (PTO Ex. 12 at 1.)

Thus, HEC's "waiver" theory is baseless. But even if the issue had not been precisely framed before trial—twice—that would not matter. "Nothing in Fed.R.Civ.P. 16 . . . 'suggests that a party waives or admits an issue as to which his opponent has the burden of proof by failing

to include the issue in his pre-trial stipulated list of remaining issues.'" *Emmons v. Southern Pacific Transp. Co.*, 701 F.2d 1112, 1118 (5th Cir. 1983) (citation omitted). HEC has always had the burden to show Kappos 2006 was prior art. It has failed to carry that burden.

B. HEC Failed to Show That Kappos 2006 Discloses the Claimed Invention, or Is Enabled

Even if Kappos 2006 were prior art, HEC's anticipation attack would still fail. The abstract describes parts of an upcoming placebo-controlled Phase III clinical trial, in which the 0.5 mg daily dose would be tested *for the first time* in human RRMS patients. (NFOF 59–60.) Kappos 2006 thus describes a test, not the claimed treatment. Kappos 2006 fails also to exclude a loading dose as the Patent requires, or to enable use of the 0.5 dose for the purpose of treating RRMS.

1. Kappos 2006 Describes an Upcoming Test, not the Claimed Treatment

The 405 Patent's defining feature was that 0.5 mg daily of fingolimod could be used to treat RRMS. The Court accordingly construed the claims to require the administration of 0.5 mg fingolimod daily for the purpose of treating RRMS, as HEC agrees (at 34–35).[14] HEC agrees also that, to prove anticipation, it must show that "every element of the claim is described, either expressly or inherently," in Kappos 2006. (HCOL 32.) HEC cannot show this.

As this Court found in the PI decision, "Kappos 2006 is a test, not a method of treatment. At [the time of] its publication date, the .5 milligram dose of fingolimod had never been used on a human MS patient. Nobody knew it would be an effective treatment, and no clinician would have

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[14] HEC says that only claim 3's preamble is at issue. (HEC Br. at 35 n. 3.) That is not true. Kappos fails to disclose either the broad "treating" purpose of claim 3, or the narrower "reducing, alleviating, or preventing" relapse purpose of claim 1, or the "slowing progression" purpose of claim 5. The experts made that clear at trial. (NFOF 77, 151–162.)

prescribed it for an RRMS patient, including candidly defendants' clinical expert, Dr. Hoffman." (D.I. 583 at 4.) The Court thus concluded that Kappos 2006 "does not disclose and does not anticipate the treatment limitation of the asserted claims of the '405 [P]atent[,]" a conclusion supported by evidence like the "ethical concerns and even opposition to testing such a low dose on human RRMS patients, including Dr. Lublin's own hospital refusing to participate in the study and the unusual futility analysis required after six months of the test." (*Id*.)

While the PI ruling is not binding here, it is persuasive authority. (NCOL 20.) Yet HEC does not even acknowledge the ruling's existence, much less attempt to say what has changed. Nothing has. Dr. Lublin and others testified that Kappos 2006 described only a placebo-controlled test, not a treatment. (NFOF 151–62.) Dr. Lublin explained that (i) the 0.5 mg dose had never been tested in RRMS patients before (*id*. 59); (ii) Phase III trials regularly fail, especially in neurology (*id*. 51); (iii) doctors were skeptical of even testing the dose (*id*. 52–55); (iv) Novartis adopted a novel futility protocol for the 0.5 mg dose because it had never before been given to an RRMS patient (*id*. 56); but (v) Mt. Sinai still balked at one of the trials because the 0.5 mg dose had never been tested before (*id*. 57). Further, Drs. Steinman and Jusko testified that a person of skill would have thought the 0.5 mg dose unlikely to work based on prior art transplant and EAE studies (*id*. 27–33, 45–47)—a conclusion the Patent Office agreed with in the IPR (*id*. 79).

Nevertheless, HEC asserts (at 35–36) that "any reasonable reader would have readily understood that Kappos discloses [a] method for treating RRMS," because the trial's "intent" was to reach certain clinical endpoints reflective of treatment. Kappos 2006 itself plainly states that the objective of the clinical trial was "to further *evaluate* efficacy and safety of fingolimod in patients with RRMS." (DTX-47.00002 (emphasis added).) That is testing, not treatment. Dr. Lublin—a clinical trial expert personally involved in the trials at issue—testified that the endpoints

were parameters to define the data obtained from running the trial, and that they have nothing to do with treatment. (NFOF 151.) The purpose of the trial is to test. (*Id.* 151–53.) Dr. Aradhye, who ran the Phase III trials for Novartis, said essentially the same thing, as did Dr. Calabresi. (*Id* 153–54.) Furthermore, as Drs. Lublin and Hoffman agreed, the study was placebo-controlled, so a person of skill would understand that patients must consent *not* to expect treatment. (*Id.* 162.)

HEC contends (at 36) that the Court's claim construction renders the dose's unknown efficacy in June 2006 irrelevant. But Dr. Lublin explained the relevance to the claimed treatment purpose in response to a question from the Court:

> THE COURT: Are you saying that efficacy is part of your analysis of anticipation of this patent?
>
> THE WITNESS: So let me clarify what I meant. To have a treatment purpose, you have to have a reason to give that treatment. That reason is based on some data showing you that can have an effect. Otherwise, you can theoretically have a treatment purpose with Tylenol for every disease. You have to know that it's going -- have some confidence that it's going to do what you want it to do. It doesn't mean it would work for every person, but there has to be evidence that it could have an effect.

(Tr. 287:17–288:6.) Dr. Hoffman had a similar take. Although he tried to backtrack at trial, Dr. Hoffman could not escape his deposition, where he admitted he would not have used 0.5 mg to treat patients in June 2006 because he "wouldn't know whether it was effective or not." (NFOF 160.) The Court employed similar reasoning in the PI—Kappos 2006 lacked a treatment purpose because "[n]obody knew it would be an effective treatment," and thus "no clinician would have prescribed it for an RRMS patient, including candidly defendants' clinical expert, Dr. Hoffman." (D.I. 583 at 4.) Thus, contrary to HEC's theory, Dr. Lublin applied the Court's claim construction exactly as the Court itself did before.

HEC argues in the alternative that, even if not explicit, using 0.5 mg for the purpose of treating RRMS is somehow "inherent" in Kappos 2006, rendering "irrelevant" the dose's unknown

efficacy in June 2006. (HEC Br. 36–37.) This makes no sense. To be "inherent," a claim element must "necessarily" be disclosed in the reference, as HEC agrees. (HCOL 41.) A treatment purpose was not "necessarily" present in Kappos 2006 for the same reasons described above.

In support of its inherency argument, HEC cites (at 36–38) *In re Montgomery*, 677 F.3d 1375 (Fed. Cir. 2012), a case HEC unsuccessfully cited also in its opposition to the PI. (D.I. 458 at 13–14.) The case was, and remains, inapposite. The method claims in *Montgomery* required actual efficacy, not a treatment purpose. 677 F.3d at 1378–81. The court found that a clinical trial summary's description of the method inherently anticipated efficacy, but *not* based on the trial's results—those "were not published until after [the] priority date and thus [were] irrelevant to an anticipation analysis." *Id*. at 1378. Rather, the court relied on pre-priority date information to find inherency. *Id*. at 1382 n. 12. Any other analysis would have turned a mere invitation to investigate into an anticipatory reference. *Id*.

Here, unlike in *Montgomery*, the allegedly anticipatory reference affirmatively *excludes* a claimed element, the method's treatment purpose. Moreover, HEC argues inherency based on the Phase III trial's results—exactly what *Montgomery* says is wrong. The 0.5 mg dose was not at an advanced stage of testing in RRMS as in *Montgomery*—it had never been tested in RRMS at all. (NFOF 59.) The absence of data made doctors skeptical of even testing the 0.5 mg daily dose (as Dr. Lublin testified). Worse, the available data taught the dose was unlikely to be effective (as Drs. Steinman and Jusko testified and the Patent Office agreed).[15] (NFOF 27–33, 45–47, 79.) In

[15] HEC argues (at 38) that skepticism and teaching away are "irrelevant" to anticipation. But Kappos 2006 must be read from the perspective of a person of skill. (HCOL 41.) The prior art would surely inform that person's view that Kappos 2006 did not describe 0.5 mg as a treatment. HEC complains also that the skepticism Dr. Lublin described was not public, but that it not the point—the skepticism illustrates how actual persons of skill viewed even testing the dose, much less using it for the purpose of treating RRMS as the claims require.

these circumstances, HEC has come nowhere close to showing anticipation by clear and convincing evidence, just as the Court predicted when granting Novartis's PI motion.[16]

2. Kappos 2006 Leaves Open the Possibility of a Loading Dose

Kappos 2006 is also missing another part of the claims—that 0.5 mg daily be administered "absent an immediately preceding loading dose regimen." (JTX-001 at 12:49–13:9.)

HEC agrees Kappos 2006 is silent on loading doses (HFOF 111–12), but argues (at 39) that the absence of a loading dose is inherent. The Court found in the PI that a person of skill would not "read the one-page, approximately 600-word abstract as inherently and necessarily excluding a loading dose[,]" and that as such "Kappos 2006 . . . does not exclude an immediately preceding loading dose." (D.I. 583 at 5.) Trial only bolstered that finding. As discussed *supra* Section I.B.2, the testimony at trial showed that a person of skill would read a 600-word abstract and a patent with very different expectations about completeness of information, and in particular, would expect a patent but not necessarily an abstract to describe a loading dose if one were given. Dr. Lublin also explained that other abstracts on fingolimod transplant experiments had also been silent on loading doses, but the full papers written and published later showed loading doses had in fact been used. (NFOF 166.) In this context, a person of skill could not rule out the possibility of a loading dose in the RRMS Phase III trial regimen based on Kappos 2006 alone.

In an attempt to support this position, HEC cherry picks testimony from Drs. Lublin and Steinman that loading doses generally are not used for approved disease modifying therapies

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[16] HEC also cites *Eli Lilly & Co. v. Teva Pharm. USA, Inc.*, 619 F.3d 1329 (Fed. Cir. 2010), to say that "if an applicant has initiated human clinical trials for a therapeutic product or process, Office personnel should presume that the applicant has established that the subject matter of that trial is reasonably predictive of having the asserted therapeutic utility." (quoting MPEP § 2107.03 at IV). But *Eli Lilly* addresses the minimal "utility" requirement of 35 U.S.C. § 101, and has no relevance to inherency for purposes of anticipation.

(HFOF 113–14). This is beside the point. Kappos 2006 describes an experiment with a never-before-tested dose of a drug that in other experiments had been used with loading doses. An experimental dosing regimen for one disease modifying drug need not adhere to the final approved regimen of a different drug. Moreover, even if a person of skill would think a loading dose unlikely, that would not "necessarily" exclude a loading dose. "Inherency . . . may not be established by probabilities or possibilities." *Cont'l Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991) (citations omitted). As an abstract, Kappos 2006 is simply too abbreviated to definitively answer the question.

HEC touts that Dr. Hoffman testified at one point that a person of skill would think a loading dose an "impossibility" in this context (HEC Br. 39), but at another point, Dr. Hoffman said the opposite. (NFOF 169.) Further, Dr. Hoffman agreed that Kappos 2006 is just a short abstract that necessarily would leave out important information about the Phase III trial—including information material to the drug's efficacy and safety. (*Id*. 165.) On this record, HEC falls far short of clear and convincing evidence that the absence of a loading dose was inherent in Kappos 2006.

3. Kappos 2006 Would Not Enable Treatment with 0.5 mg in June 2006

HEC's Kappos 2006 attack fails for a final reason—the abstract did not enable the use of 0.5 mg daily to treat RRMS. HEC agrees that anticipatory references must be enabled. (HCOL 48.) HEC agrees also that, to be enabling, Kappos 2006 must teach a person of skill "how to 'make and use' the invention." (*Id*. 50.) If "undue experimentation" under *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) would be needed, then the reference does not enable the invention. *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009) (citing *Impax Labs., Inc. v. Aventis Pharms. Inc.*, 545 F.3d 1312, 1314 (Fed. Cir. 2008)). So it is here.

HEC failed to address *Wands* and undue experimentation at trial, or in briefing. That failure alone is fatal. As Dr. Lublin testified, Kappos 2006 would not permit a person of skill to use 0.5 mg daily for the purpose of treating RRMS without undue experimentation. (NFOF 171–74.) Every pertinent *Wands* factor shows that Kappos 2006 is not enabled. (*Id.*) Dr. Hoffman himself admitted that he would not have given 0.5 mg daily to his patients in June 2006 because he would not know the dose would work.

On point are the Court's opinions in *GlaxoSmithKline LLC v. Glenmark Pharm. Inc., USA* ("*GSK*"), which Novartis highlighted in the PTO (at Ex. 4, ¶ 47), and which were briefed and relied upon by the Court in the PI (D.I. 358 at 16, D.I. 583 at 5), but which HEC completely fails to address now. In *GSK*, defendants argued that "Kelly"—a prior announcement of a Phase III trial on the claimed treatment method—anticipated. The court rejected the argument on summary judgment, where it found that "a planned but not yet started trial" was "too theoretical" to be enabling as a matter of law, even though the protocol "discuss[ed] some evidence suggesting that the treatment to be provided in the planned trial may be effective." No. CV 14-877-LPS-CJB, 2017 WL 8944995, at *21 (D. Del. May 2, 2017), *report and recommendation adopted*, No. CV 14-877-LPS-CJB, 2017 WL 2290141 (D. Del. May 25, 2017). The court thus found that "[t]here is a fact question as to whether Kelly's disclosure of a planned (but not initiated) trial was sufficiently concrete to truly put the content of that study in the possession of the public." *Id*. At trial, the jury found for the patent owner on this question, *GlaxoSmithKline LLC v. Teva Pharm. USA, Inc.*, 313 F. Supp. 3d 582, 585 (D. Del. 2018); and the court found that verdict amply supported in denying JMOL as to validity. *Id.* at 599.

The parallels here are inescapable, as the Court observed in the PI ruling. (*See* D.I. 583 at 5 (observing that Novartis's "analogy to our *GSK* case is a persuasive comparison, and

[D]efendants' efforts to distinguish *GSK*, which only came up today, appear likely to fail").) Indeed the Kelly reference in *GSK* contained more enabling information than Kappos 2006—it described positive Phase II results for the claimed method. Kappos 2006 does not. The 0.5 mg dose had never been tested before, as a person of skill would have understood when reading Kappos 2006. (NFOF 59.) Moreover, here the prior art suggested that the 0.5 mg dose would not work, as the Patent Office found. (*Id*. at 27–33, 45-47, 79.) Doctors in June 2006 were skeptical of even testing the dose in Phase III, much less actually using the dose to treat patients. (*Id*. at 52–58.) In these circumstances, the *Wands* factors point definitively away from Kappos 2006's enablement. *See, e.g.*, *In re Hoffmann*, 558 F. App'x 985, 987 (Fed. Cir. 2014) (applying *Wands* factors to find no enablement when "the very efficacy of the method itself is subject to considerable doubt in the scientific community").

HEC cites (at 40) *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318 (Fed. Cir. 2005), to assert that "the effectiveness of the prior art is not relevant." Nothing in *Rasmusson* conflicts with *GSK*; indeed, the court cited *Rasmusson* in *GSK* but still found Kelly not enabled. *See GSK*, 2017 WL 8944995, at *19–21. Presumably, that is because, unlike the claims in *Rasmusson*, the claims in *GSK* required using the method for a treatment purpose, and the Court found that Kelly did not enable a doctor to use the method as a treatment. As in *GSK*, the Patent here claims a treatment purpose. Kappos 2006 does not enable that purpose.

CONCLUSION

For the reasons set forth above, the Court should issue a judgment that claims 1–6 of the 405 Patent are not invalid and enforceable, and an order dismissing Defendants' Counterclaims with prejudice.

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